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CASE REPORT

Eosinophilia à deux: a brain nagging souvenir from the Philippines

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Abstract *Angiostrongylus cantonensis* is the most common cause of eosinophilic meningitis. Although a rare condition among travelers, increased travel and global transportation of food products may result in more cases across non-endemic, developed countries in the future. We here describe two men with headache and painful skin after visiting the Philippines as presenting symptoms. Subsequently, confusion and focal neurologic symptoms developed. Both had increased serum eosinophils; however, CSF eosinophilia was only demonstrated after repeated lumbar puncture. In the CSF of both, *Angiostrongylus* spp. DNA was detected. Both were treated with albendazole combined with corticosteroids, after which symptoms improved.

Case report

In March 2014, two Dutch male patients (A and B), age 45 and 49 years, respectively, presented at our outpatient clinic 7 days after returning from a 2-week holiday in the Philippines. Patient A complained of headache and painful skin of the upper legs, patient B of one painful skin area on the chest. There were no other complaints. Both had eaten fresh fish (caught the same day, including whole barracuda), prawns, salads and raw vegetables. They denied eating snails or slugs. Both patients were HIV positive, but had undetectable viral loads on antiretroviral treatment and stable CD4-counts, greater than 500×10^6/L.

Neurological examination showed dysesthesia on chest and upper legs. Physical examination was otherwise normal, both were afebrile. Laboratory examination showed serum eosinophilia (1.26 and 0.66 $\times$ 10^9/L in patients A and B, respectively) with otherwise normal leukocyte differentiation. A parasitic infection was suspected; however, no parasites were found with feces microscopy for ova and parasites and PCRs for *Giardia*, *Entamoeba histolytica*, *Cryptosporidium*, *Dientamoeba*, and *Blastocystis* sp. Serology was negative for *Filaria, Strongyloides, Schistosoma, Fasciola* and *Toxoplasma.*

Five days later, patient A presented with confusion and diplopia. On examination he was disorientated and there was paralysis of the abducens nerve. Lumbar puncture (LP) showed a raised opening pressure of 37 cm water, pleocytosis (1323 leukocytes/uL^3), elevated protein (1.53 g/L), and normal glucose (2.59 mmol/L); there was no eosinophilia (<0.001 $\times$ 10^9/L). MRI of the brain showed a subtle hyperintense left pontine lesion (see Fig. 1), without leptomeningeal enhancement.

He was admitted with a clinical diagnosis of meningoencephalitis, and empirical treatment for bacterial and herpes virus-encephalitis was started. Examination of CSF with Gram stain, culture and PCR for bacteria and viruses remained negative, upon which treatment was stopped. Because of the travel-related presentation, peripheral eosinophilia and meningo-encephalitis, a parasitic infection was still suspected. A repeated LP after 5 days showed increased pleocytosis (2619 leukocytes/uL^3), with CSF eosinophilia (0.059 $\times$ 10^9/L). At this time, patient B presented with progressive pain and loss of strength of his left

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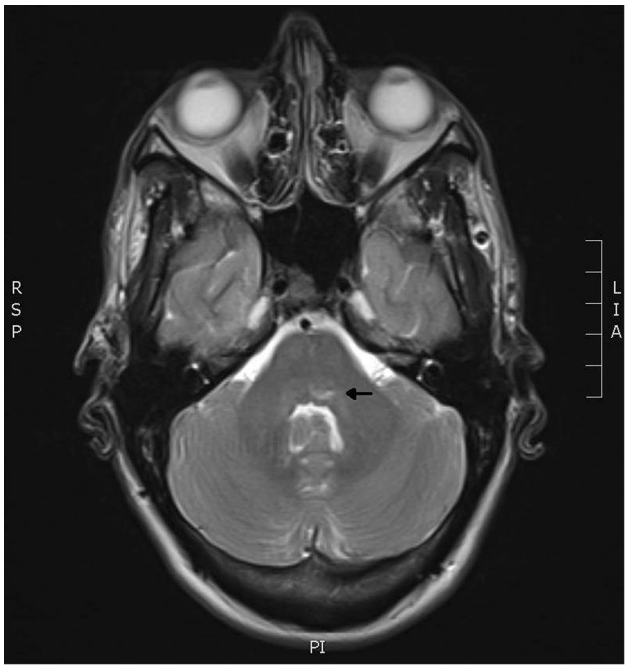

Fig. 1 Hyperintense lesion on T2-FLAIR, gadolinium-enhanced image, in the left pontine tegmentum of patient A

arm. LP showed pleocytosis (2442 leukocytes/uL^3), without eosinophilia.

Now, with the clinical diagnosis of eosinophilic meningo-encephalitis, albendazole (600 mg bid) was started combined with prednisolone (20 mg tid) in both patients, after which both patients improved within weeks without prior worsening of symptoms. Serum eosinophilia disappeared within 2 weeks, the pain disappeared within 1 month, but the altered cutaneous sensations are present to date in both patients.

Experimental real-time PCRs performed in our laboratory according to Qvarnstroms et al. [1] on CSF samples of both patients turned out positive for *Angiostrongylus cantonensis*. Specificity of the PCR was confirmed by sequencing the 106 bp amplicons, which proved identical to *Angiostrongylus cantonensis* sequences [1], except for an insertion of a single nucleotide.

Helminthic infections are the most common cause of eosinophilic meningo-encephalitis, and the differential diagnosis includes angiostrongyliasis, gnathostomiasis, baylisascariasis, toxocariasis and neurocysticercosis [3, 4]. *Angiostrongylus cantonensis*, is the principal cause of eosinophilic meningitis worldwide [2]. Since these parasites preferably reside in the rat pulmonary arteries, they are also called "rat lungworm". Eggs hatch in the rats' lungs, and first-stage parasites are passed into rodent feces. Subsequent intermediate hosts are several species of snails and slugs, in which the worms' larvae mature into an infective stage. Paratenic or "transport-hosts" include freshwater prawns and shrimp, frogs and monitor lizards. Humans become accidental hosts by ingesting infective larvae of *Angiostrongylus cantonensis* through consumption of undercooked intermediate of paratenic hosts, and eating contaminated vegetables with snail excretions (slime) has been described as mode of transmission as well [5, 6]. Upon ingestion, the larvae migrate to the central nervous system where the larvae cannot complete their life cycle and ultimately die. Meningitis and focal neurological symptoms are the result of mechanical stress and antigens released by parasites, eliciting an eosinophilic inflammatory response.

Travelers with angiostrongyliasis often present with subacute infectious disease of the CNS. After an incubation period of 1–3 weeks, symptoms such as (frontal or bitemporal) headache, visual disturbance, vomiting, nuchal rigidity, hyperesthesia, paresthesia, and fever (less common) may develop. Like our patients, paresthesias are the most distinctive neurological finding in adults with angiostrongyliasis; symptoms may be present on the extremities, trunk, or face, and they can persist for weeks after other symptoms have resolved. Although the disease can be lethal, most infections are self-limiting.

Diagnosis is usually difficult and is based on: presence of eosinophilic pleocytosis in the CSF, a clinical history of specific food exposure and on serology. Serology tests, however, are only available in endemic areas and the gold standard for the definitive diagnosis of angiostrongyliasis remains the finding of the parasite in the CSF. Clinical suspicion is important, because repeated LP may be necessary to make the diagnosis, as illustrated by this case, where initially no CSF eosinophilia was present. Treatment of angiostrongyliasis is mainly supportive. There are no standardized recommendations, although there is evidence that 2 weeks of high-dose glucocorticoids given improves the course of disease. Anti-helminthic therapy (albendazole or ivermectin) combined with corticosteroids, was shown to shorten the median time to resolution of headache, but is still controversial [7, 8].

Although still a rare condition among travelers, angiostrongyliasis is described to be emerging worldwide, due to increased travel and global transportation of food products. This may result in more cases across non-endemic, developed countries in the future [9].

Therefore, physicians should be aware of the possibility of angiostrongyliasis in returning travelers complaining of headache or paresthesias in combination with suggestive food exposure and peripheral eosinophilia.

Conflict of interest On behalf of all authors, the corresponding author states that there is no conflict of interest.

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